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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/441,355	05/15/95	HOUGHTON	M 0063.021

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ALISA A HARBIN
CHIRON CORPORATION
INTELLECTUAL PROPERTY R440
PO BOX 8097
EMERYVILLE CA 94662-8097

EXAMINER	
ZEMAN, M	
ART UNIT	PAPER NUMBER
1815	8

DATE MAILED: 08/12/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 5/5/97

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 40-87 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 40-87 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

* U.S. GPO: 1996-410-238/40050

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1815.

Claim Rejections - 35 USC § 112

2. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 20 appears to be drawn to a particle comprising a fusion of an HCV epitope and a particle forming protein. No particular epitopes of HCV, or particular particle forming polypeptides are recited. No particular amino acid sequences are recited. No characteristics of the particle, such as size, density, or immunogenicity are recited. The metes and bounds of the phrase "immunogenic against HCV" are unclear. A particle may be immunogenic in that it can elicit specific antibodies, or it may also provide protective immunity, but it is not clear from the wording of the claim which meaning of the phrase "immunogenic against" the applicant is claiming. (i.e. elicitation of specific antibodies, or protective immunity.) The metes and bounds of the phrase "HCV epitope" are unclear. No particular epitopes are claimed, nor is there full guidance in the specification as to which portions of what proteins of HCV would elicit

antibodies when used as an immunogen, or which portions could be used to induce protective immunity. Neither the length of the epitope nor the sequences comprising the claimed epitopes are disclosed, nor are the immunological characteristics pointed out.

3. Claim 38 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 38 is drawn to a method of producing HCV specific antibodies. The method uses an immunogenic polypeptide containing an HCV epitope. The metes and bounds of the phrase "HCV epitope" are unclear. No particular epitopes are claimed, nor is there full guidance in the specification as to which portions of what proteins of HCV would elicit antibodies when used as an immunogen, or which portions could be used to induce protective immunity. Neither the length of the epitope nor the sequences comprising the claimed epitopes are disclosed, nor are the immunological characteristics pointed out. The metes and bounds of the word "isolated" in the context of purified polypeptides is unclear. No method of isolation is given, nor are there limits as to the amounts of contaminants or the presence of other proteins or polypeptides in the inoculum. As written the claim could encompass isolated viral particles, which would contain HCV epitopes.

4. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 39 is vague and indefinite as it depends from a cancelled claim, claim 11. Further, the metes and bounds of the phrase "immunogonic polypeptide" are unclear. A

polypeptide may be immunogenic in that it can elicit specific antibodies, or it may also provide protective immunity; it is not clear from the wording of the claim which meaning of the phrase "immunogenic polypeptide" the applicant is claimimg. (i.e. the elicitation of specific antibodies, or the elicitation of protective immunity.) The claim recites that the "administering is of an amount sufficient to produce an immune response." No particular amounts are given, nor are immunization schedules given. The metes and bounds of "an immune response" are unclear. As noted above, the immune response in terms of antibody production can be of two forms: the production of specific antibodies, or protective immunity. Also, an immune response can be a cell-mediated response, which would not necessarily result in the production of antibody. Clarification of the claim language is required.

5. Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. At the time of filing, and as late as 1992, none of the potential HCV vaccines had been successful in the induction of protective immunity. Farci (Farci et al 1992 Nature V 258 p 135) discusses the lack of protection against reinfection with HCV in the primate animal model, the chimpanzee. The authors speculate that the reason for the lack of protection is the inability of the host to generate an effective HCV neutralizing antibody, and the potential for the emergence of escape mutants of HCV. The specification as filed does not demonstrate the ability of the claimed

method to induce protective immunity. Viral challenge experiments are not disclosed. The pharmacologically effective dosages for any model system are not disclosed.

6. Claims 20, 32, 38 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Each of these claims uses language such as "immunogenic polypeptide" or "HCV epitope." Even though brief definitions of these terms are given in the specification, the specification does not give sufficient guidance as to what portions of what polypeptides of HCV could be immunogenic, nor does it properly teach which short amino acid sequences would qualify as an HCV epitope. At page 31, of the specification, an epitope is defined as: "an antigenic determinant of a polypeptide." It is further defined as being from 3-10 amino acids in length. There is no thorough guidance as to which 3-10 amino acid combinations would be antigenic and result in the elicitation of specific antibodies. Many amino acid sequences are disclosed in the specification as filed, however there is no indication of antigenic regions or epitopic regions, nor is there indication of which polypeptides could be immunogenic. The sequences in the disclosure and the lack of specific teaches results in an invitation to experiment with the many possible combinations of sequences to find out which portions of which polypeptides are immunogenic, or which short polypeptides could qualify as an HCV epitope.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

8. Claims 32, 38 and 39 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by any of Wands, Tabor, Tabor, Coursaget or Wands and under 35 U.S.C. 102(e) as being anticipated by any of Seto, Wands or Pillot.

Claim 32 is drawn to a polypeptide vaccine for HCV. Wands (US Patent 4,271,145) discloses the use of antigens of NANBH in the immunization of animals, with a recitation of appropriate dosages, adjuvants and dosing schedules. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Tabor (US Patent 4,356,164) discloses using NANBH polypeptides in the sera of infected patients in the immunization of chimpanzees. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Tabor (US Patent 4,395,395) discloses a NANBH antigen used as a vaccine. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Coursaget (US Patent 4,464,474) discloses the recovery of NANBH particles, and their use as a vaccine. Coursaget also discloses the use of polypeptides resulting from the destruction of the particles (as with detergents) in vaccine preparations. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Wands (US Patent 4,491,632) discloses the immunization of animals with a recitation of appropriate dosage schedules, amounts and adjuvants. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Seto (US Patent 4,673,634) discloses the use of a NANBH antigen as a vaccine. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Wands (US Patent 4,870,016) discloses the isolation of NANBH particles and their use in the immunization of chimpanzees. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Pillot (US Patent 4,871,659) discloses the use of antigens from infected patients to immunize chimpanzees. (Claim 32) The method disclosed results in the production of antibodies to NANBH. (Claims 38 and 39)

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Valenzuela inview of Seto. Claim 20 is drawn to a recombinant particle forming molecule containing an HCV epitope. Valenzuela (Valenzuela et al 1982 Nature, Vol 298 p 347) discloses the recombinant expression of HBV particles in yeast. Valenzuela (US Patent 5,098,704) discloses the production of recombinant HbsAg containing sequences from a heterologous polypeptide, and using the recombinant particles for the production of specific antibodies. Valenzuela (Valenzuela et al. 1985 Biotechnology Vol 3 p 323) discloses the construction of polyvalent vaccines that contain HbsAg and HSV epitopes. Seto (US Patent 4,673,634) discloses the isolation of NANBH angigens. It would have been obvious for one of ordinary skill in the art at the time the invention was made to have taken the technology of Valenzuela of creating particles containing a non-HCV particle forming polypeptide, and the NANBH antigen of Seto to create a particle containing an HCV epitope. Such particles were shown to be very immunogenic by Valenzuela. With the ultimate aim of attempting to create a vaccine against NANBH, at the time

the invention was made, immunogenic particles appeared to be the best method of inducing protective immunity.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marian Knode, can be reached on (703) 308-4311.

The fax number for this Art Unit is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

mkz
October 11, 1996

MICHAEL P. WOODWARD
PRIMARY EXAMINER
GROUP 1800